

FIG. 1

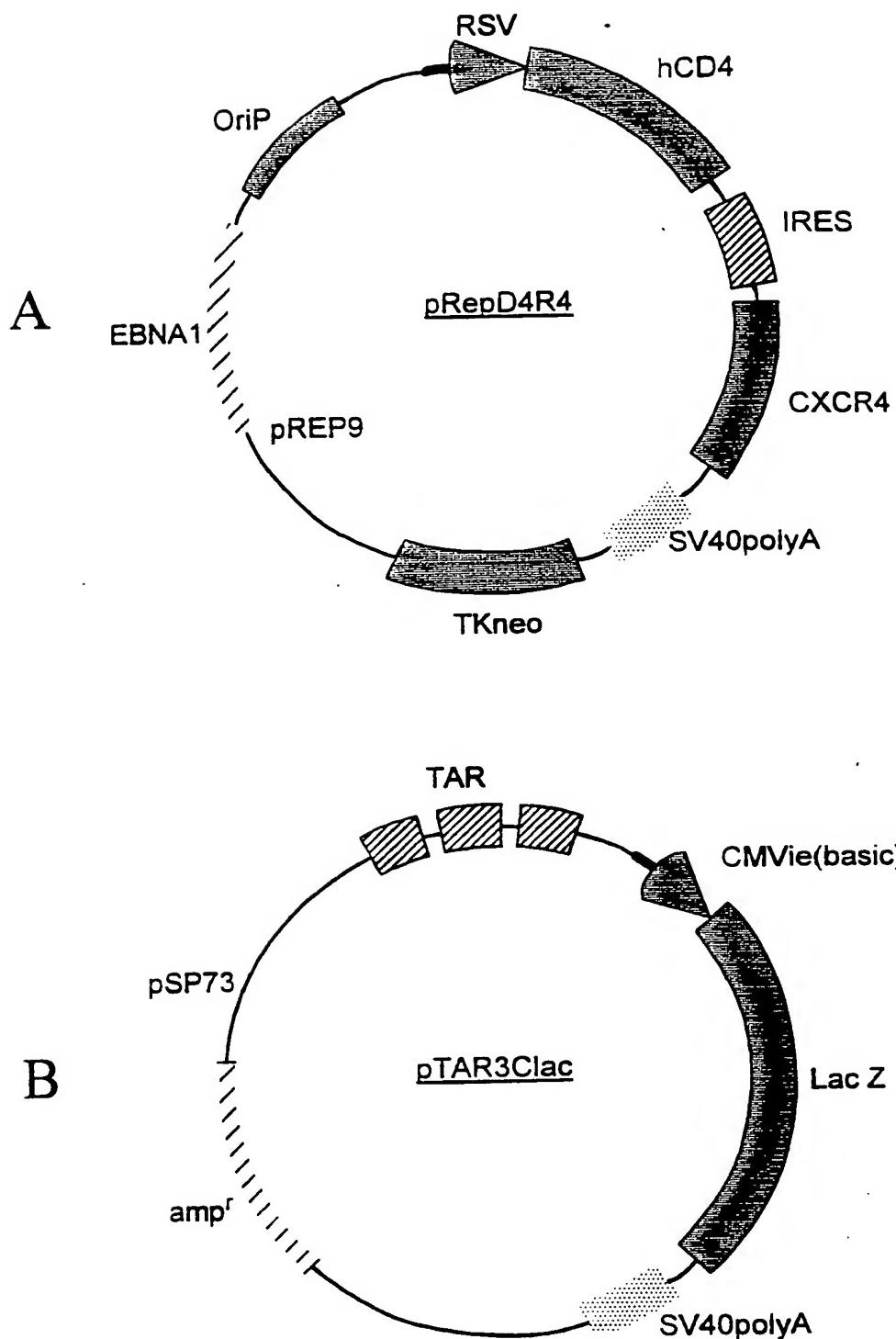


FIG. 2

FIG. 3

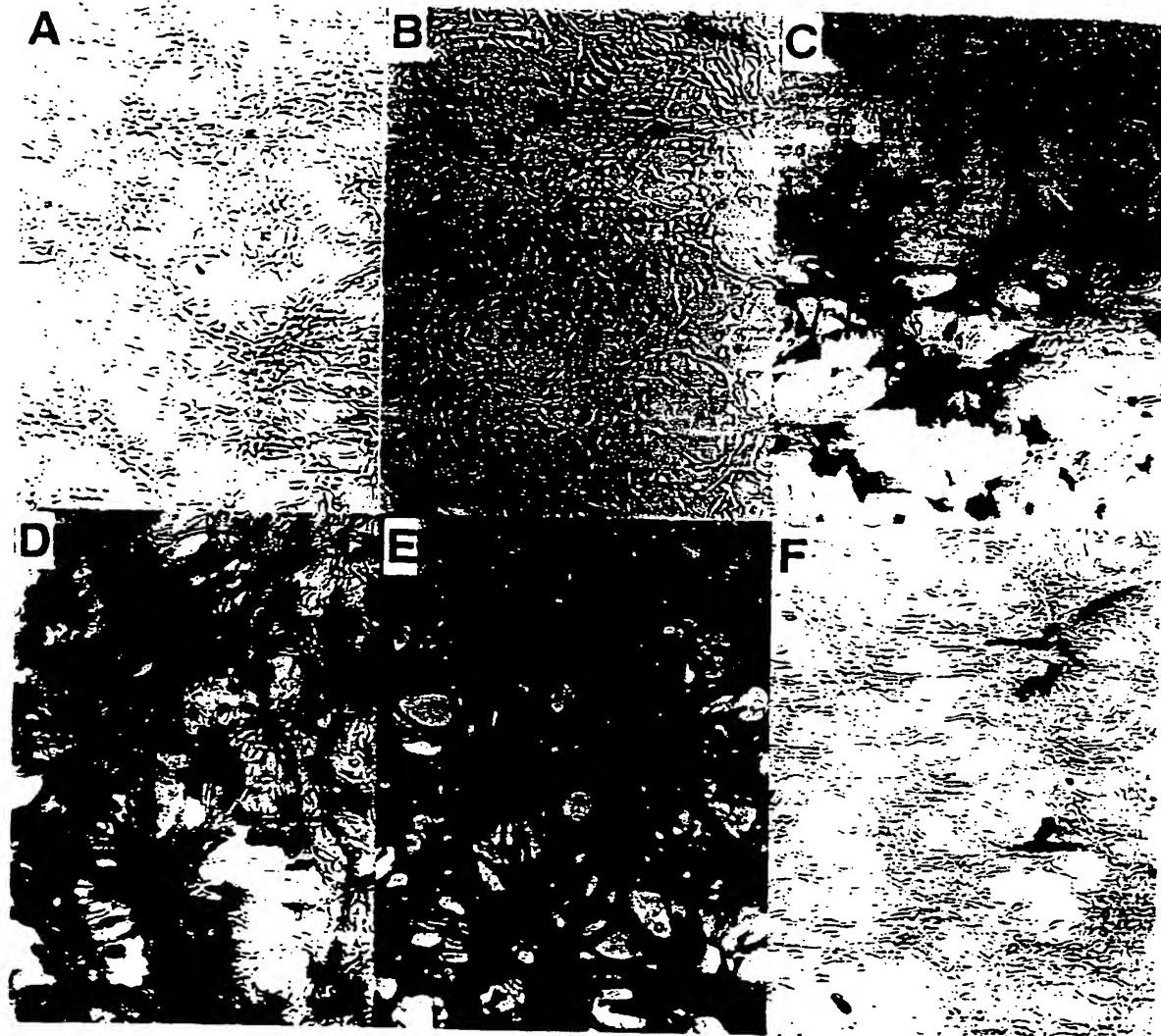


FIG. 4A

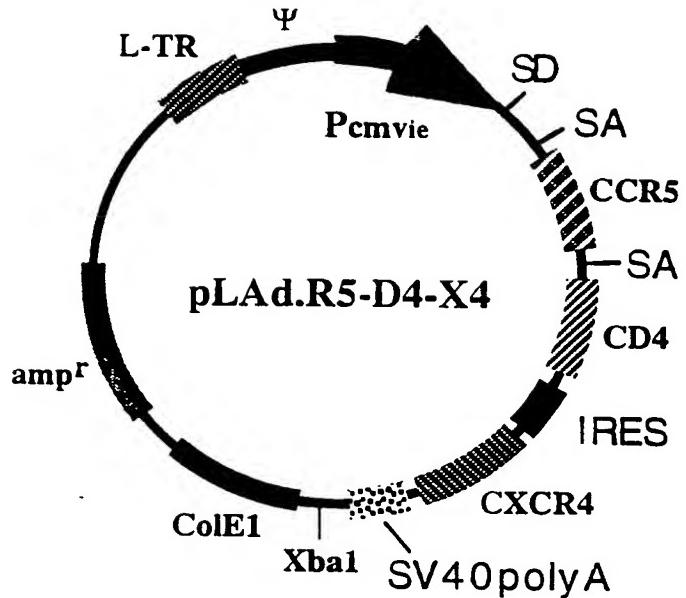


FIG. 4B

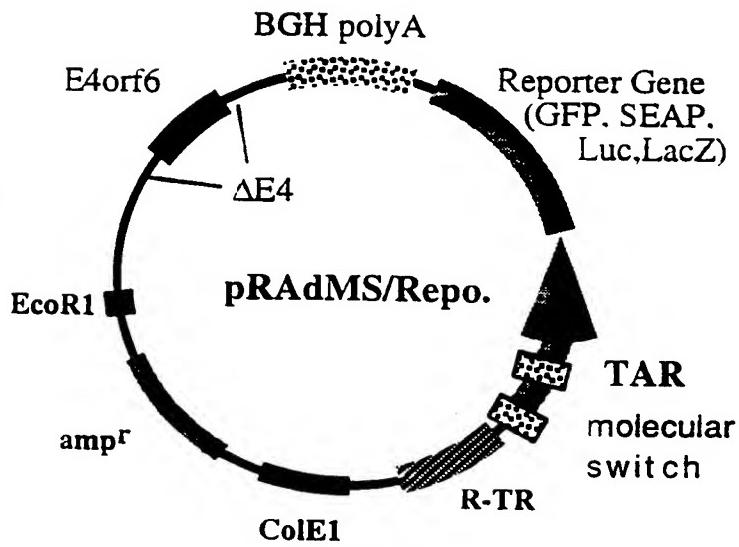


FIG. 5A

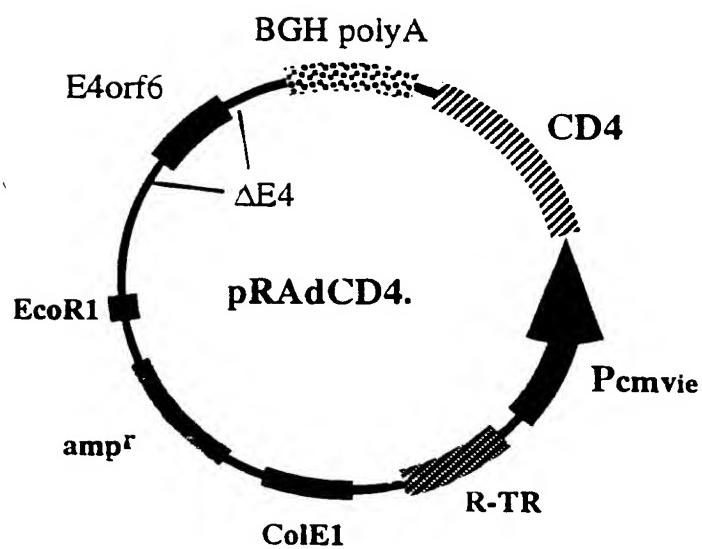
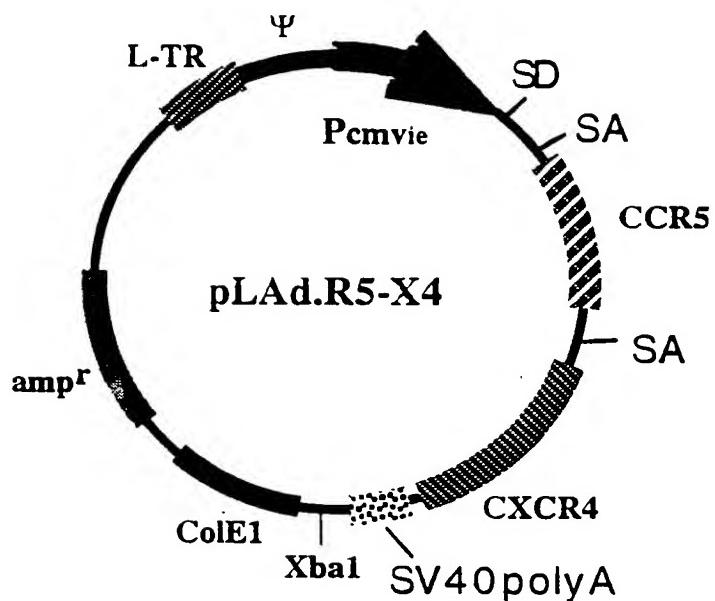


FIG. 5B

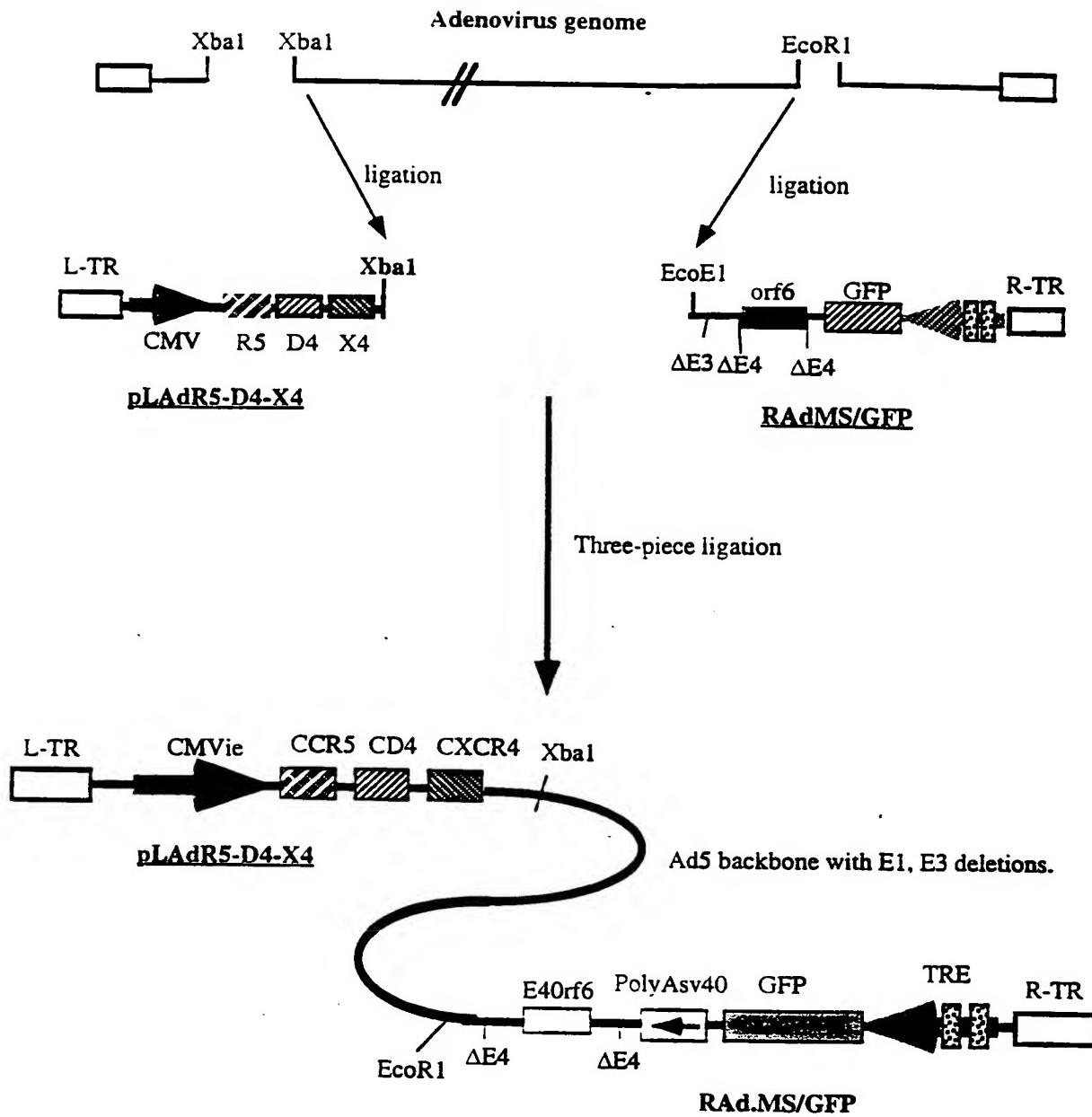


FIG. 6

pLAd-CCR5.CXCR4 (9 Kb)

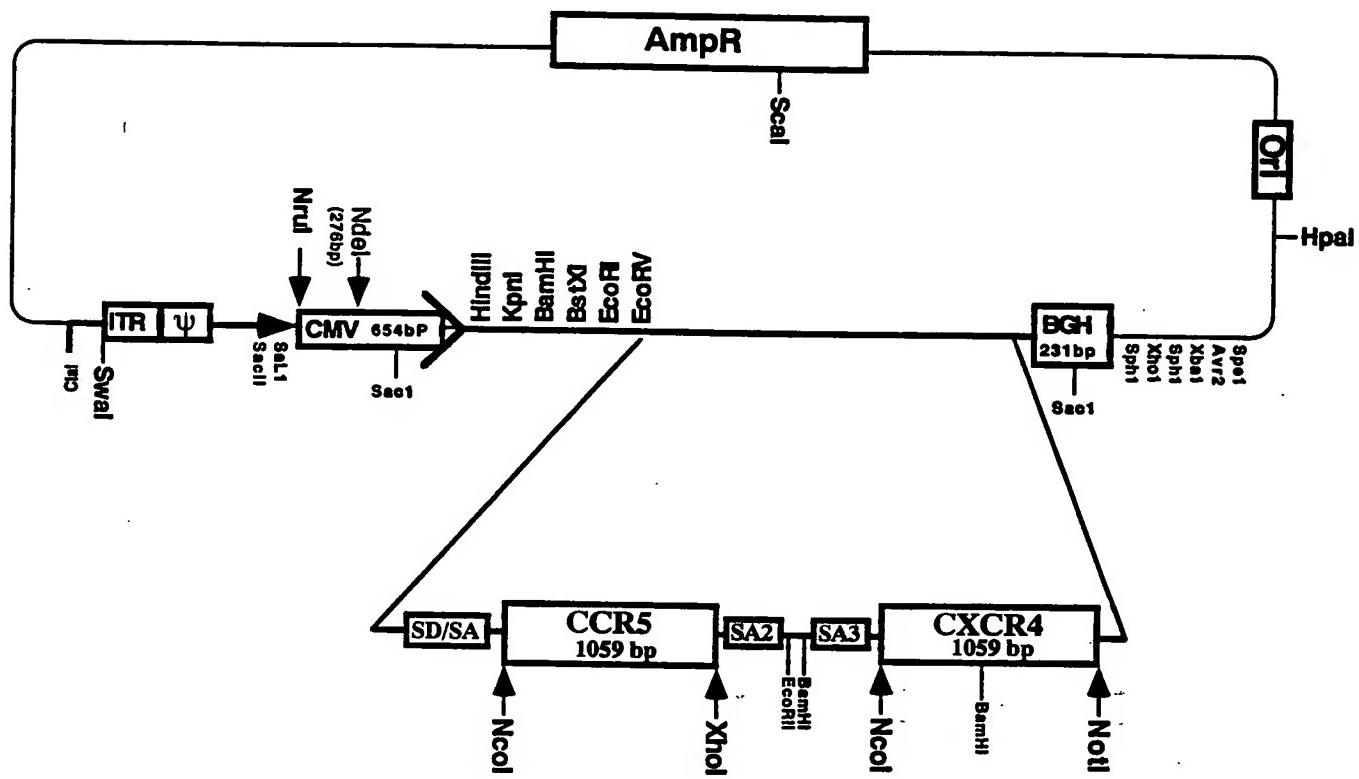


FIGURE 7A

pRAd.CMV.Fiber.ORF6-CD4.CXCR4 (~14.8 Kb)

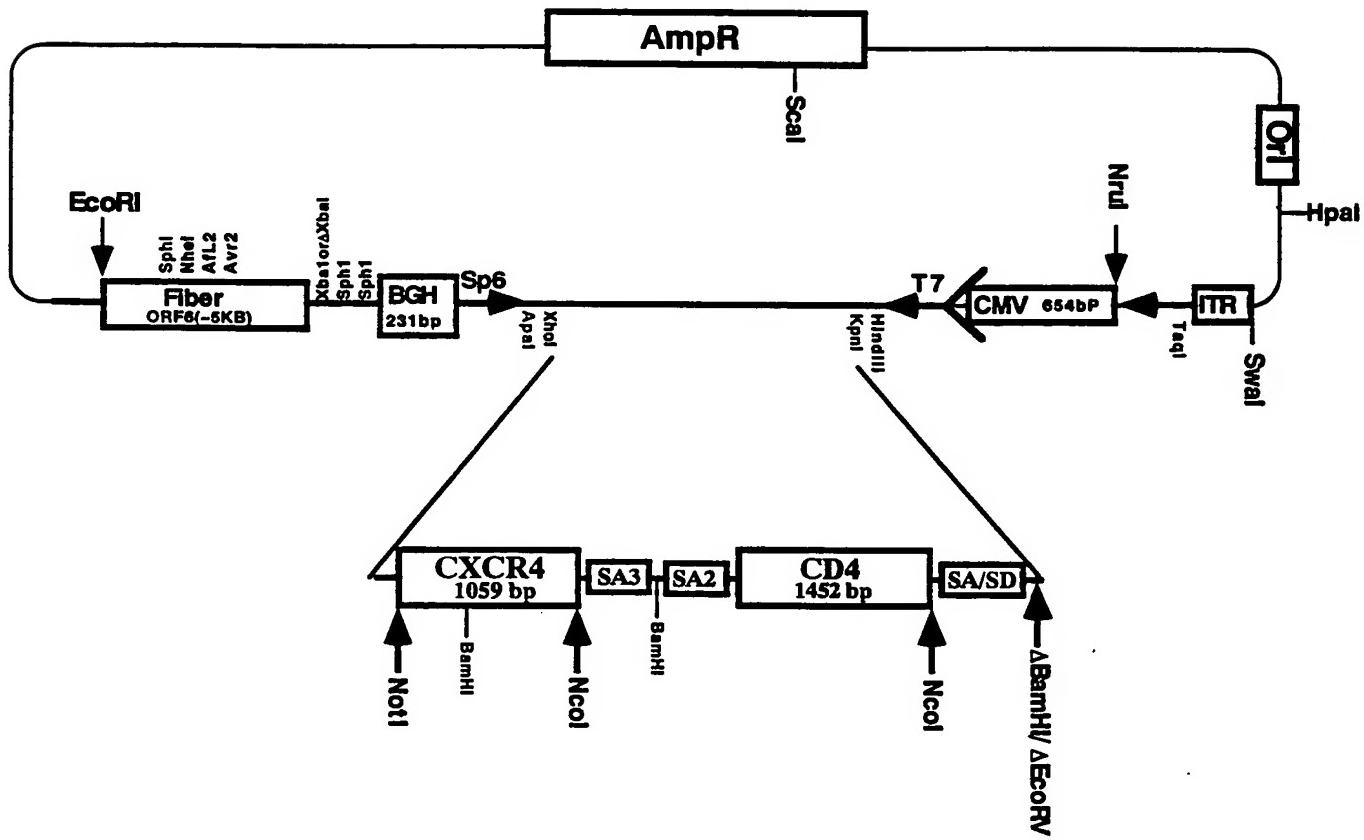
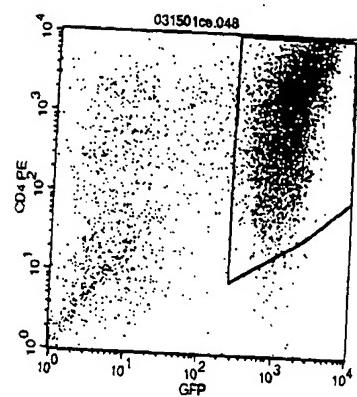


FIGURE 7B

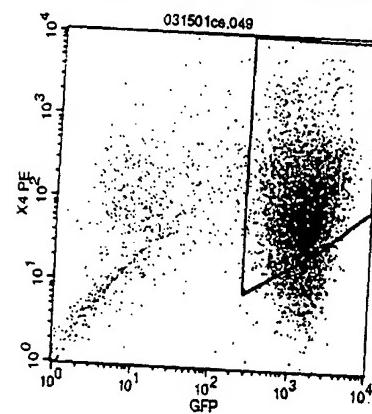
FIGURE 8

A.



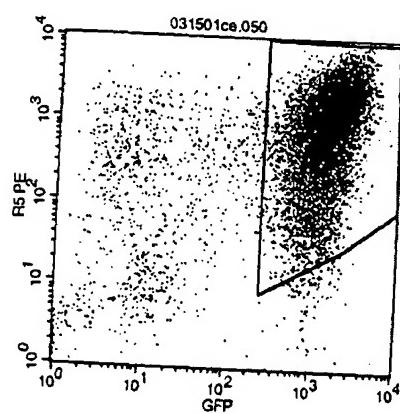
CD4 Expression Level: 84.0 %

B.



CXCR4 Expression Level: 77.7 %

C.



CCR5 Expression Level: 89.6 %

FIGURE 8

E

F

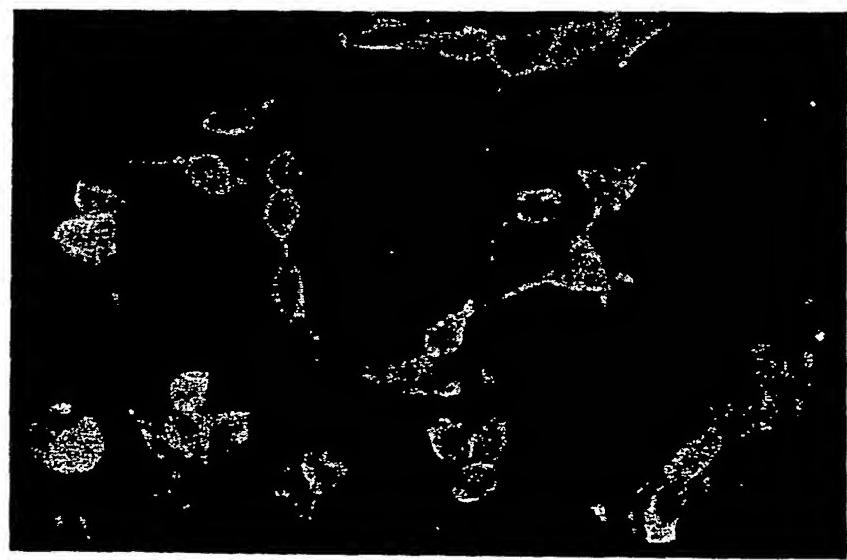
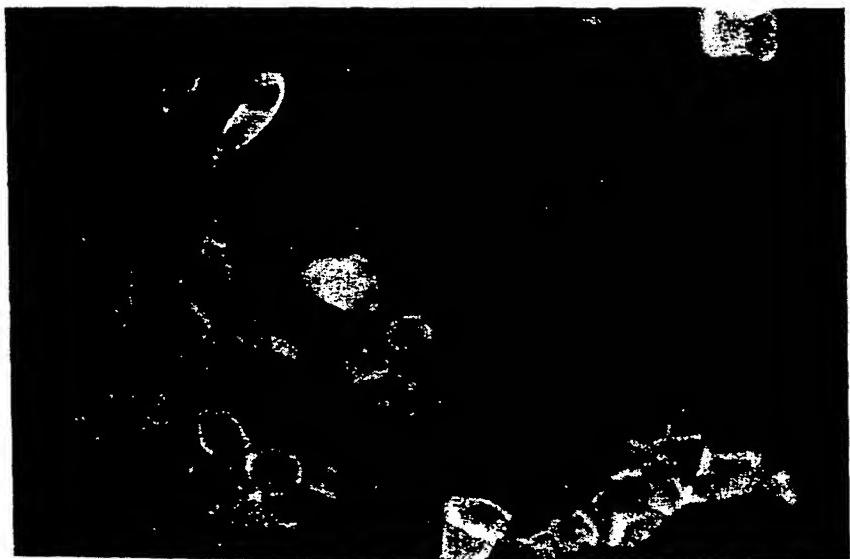


FIGURE 8G

#	Cell Types	Infected	Fluorescent-PE Ab	All %Gated	M1 %Gated	All Mean	M1 Mean	All Geo Mean	M1 Geo Mean
1	HUT78	non	mouse IgG 2ak-PE	100	1.2	4.04	21.74	3.35	18.83
2		non	CD4-PE	100	99.92	628.77	629.25	484.56	486.22
3		non	CXCR4-PE	100	65.29	24.21	32.1	18.27	26.74
4		non	CCR5-PE	100	1.56	4.14	27.48	3.34	23.44
5	CEM-NK-R5	non	mouse IgG 2ak-PE	100	3.12	3.74	19.8	3.05	16.24
6		non	CD4-PE	100	99.6	343.3	344.67	285.47	290.65
7		non	CXCR4-PE	100	98.99	65.93	66.55	53.8	55.13
8		non	CCR5-PE	100	66.66	38.76	55.64	16.91	32.66
9	Molt-4-R5	non	mouse IgG 2ak-PE	100	1.15	3.87	31.78	3.31	20.82
10		non	CD4-PE	100	57.1	35.1	57.41	15.58	39.05
11		non	CXCR4-PE	100	91.44	73.1	79.25	47.6	57.08
12		non	CCR5-PE	100	59.66	37.1	57.94	17.75	38.66
13	CEM-A	non	mouse IgG 2ak-PE	100	0.59	3.38	14.07	3.01	12.31
14		non	CD4-PE	100	94.44	98.93	104.5	62.23	73.75
15		non	CXCR4-PE	100	99.69	87.06	87.31	69.86	70.36
16		non	CCR5-PE	100	0.24	3.06	33.62	2.7	17.45
17	MEGL	non	mouse IgG 2ak-PE	100	2.1	6.17	19.43	5.45	18.61
18			CD4-PE	100	96.7	126.69	130.76	97.19	106.47
19			CXCR4-PE	100	50.34	16.25	22.6	14.18	21.27
20			CCR5-PE	100	2.03	6.34	20.31	5.62	19.43
21	Indicator#44	3R122900	mouse IgG 2ak-PE	100	1.86	4.96	27.72	4.16	19.95
22	MOI, 30		CD4-PE	100	95.19	577.67	584.4	271.07	324.48
23			CXCR4-PE	100	95.78	177.72	185.15	108.28	121.08
24			CCR5-PE	100	92.42	258.22	278.69	132.99	167.66
25	Indicator#44	3R122900	mouse IgG 2ak-PE	100	2.08	5.11	32.83	4.21	23.34
26	MOI, 60		CD4-PE	100	93.42	894.83	957.23	393.37	518.33
27			CXCR4-PE	100	93.68	219.61	233.8	125.85	150.97
28			CCR5-PE	100	91.64	369.08	401.96	175.48	232.68

FIGURE 8G - Cont.

#	Cell Types	Infected	Fluorescent-PE Ab	All %Gated	M1 %Gated	All Mean	M1 Mean	All Geo Mean	M1 Geo Mean
29	HeLa	non	mouse IgG 2ak-PE	100	1.09	3.85	34.76	3.06	23.76
30		non	CD4-PE	100	1.28	5.05	28.9	4.22	19.37
31		non	CXCR4-PE	100	94.37	69.86	73.42	53.53	59.26
32		non	CCR5-PE	100	2.1	5.29	21.55	4.45	18.95
33	PBMC	non	mouse IgG 2ak-PE	100	0.13	4.02	237.03	2.89	164
34		non	CD4-PE	100	42.6	315.27	731.4	37.45	655.64
35		non	CXCR4-PE	100	20.35	35.15	101.11	18.07	89.8
36		non	CCR5-PE	100	0.24	4.88	316.55	3.03	180.47

FIGURE 9

A.



B.



C.

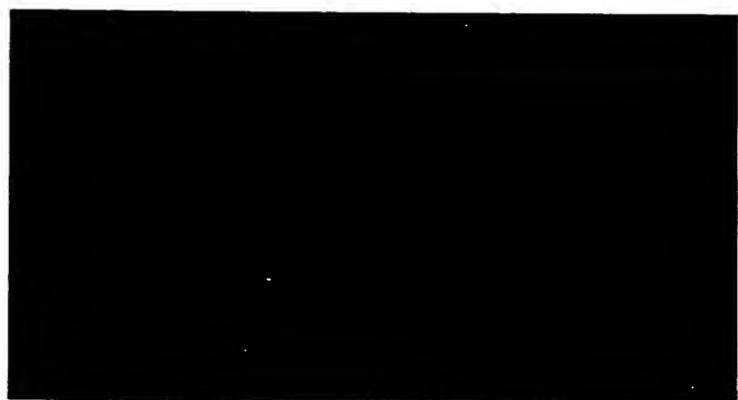


FIGURE 10

Table 1. Viral infection of Indicator Cells by HIV-1 Subtypes

Cat. No.	Inhibition by IIIB Ab (4 µl)	Subtype (gag/env)	Viral Titer (ip/ml)	Co-receptor	NIH p24 (ng/ml)	Phenotype
398	(HTLV-IIIB/H9) 100% (50 ip) 88% (225 ip) 83% (400 ip)	B/B	2.0×10^5	X4	-	SI (+++)
1650	(92UG029) 16% (170 ip) 35% (600 ip)	A/A	8.9×10^3	X4	47	SI (+)
1996	(93RW002)	/A	1.9×10^2	R5	121	SI
2304	(94UG103) 29% (37 ip) 12% (185 ip)	/A	3.7×10^3	R5,X4	155	SI (++)
1658	(92TH014)	B/B	1.2×10^4	R5	177	SI
2308	(93BR012) 16% (120 ip) 38% (660 ip)	/B	1.2×10^4	R5	316	SI (+)
1777	(92BR025) 8% (120 ip) 10% (500 ip)	C/C	1.0×10^4	R5	164	NSI*(±)
4164	(98CN006)	C/C	8.8×10^3	R5	160	SI
1684	(92UG005) 23% (400 ip) 22 % (1200 ip)	D/D	1.7×10^4	R5	225	SI (+)
1952	(93UG065)	D/D	1.6×10^3	X4	245	SI
2166	(93TH053)	/E	1.4×10^3	X4	45	NSI*
2167	(93TH054)	/E	2.4×10^3	R5	58	SI
2314	(93BR019) 40% (86 ip) 23% (430 ip)	/BF	8.6×10^3	X4	128	SI (++)
2329	(93BR020)	F/F	5.7×10^3	R5, X4	169	SI
2338	(93BR029) 33% (300 ip)	B/F	5.8×10^3	R5	185	SI (+++)
4143	(BCF13) 32% (180 ip)	Group O	2.9×10^4	-	-	SI (+++)

All viruses were titrated between day 3 and day 4 postinfection

* At day 4, there were no syncytial formed.

FIGURE 11

Comparison GenPhar Indicator with MAGI Cells					
HIV	HIV Strains	Sources	Catalogue	Co-Receptor	Indicator#44 (Ip/ml)
Wild type	IIIB	NIH	398	X4	75,000
Patient's Isolates	JM	GenPhar, INC	X4		1,050
Patient's Isolates	92UG001	NIH	1647	X4, R5	
Patient's Isolates	93TH054	NIH	2167	R5	5,200
Patient's Isolates	93BR020	NIH	2329	X4R5	4,800
					0
					5,250
					530
					9.91

FIGURE 12

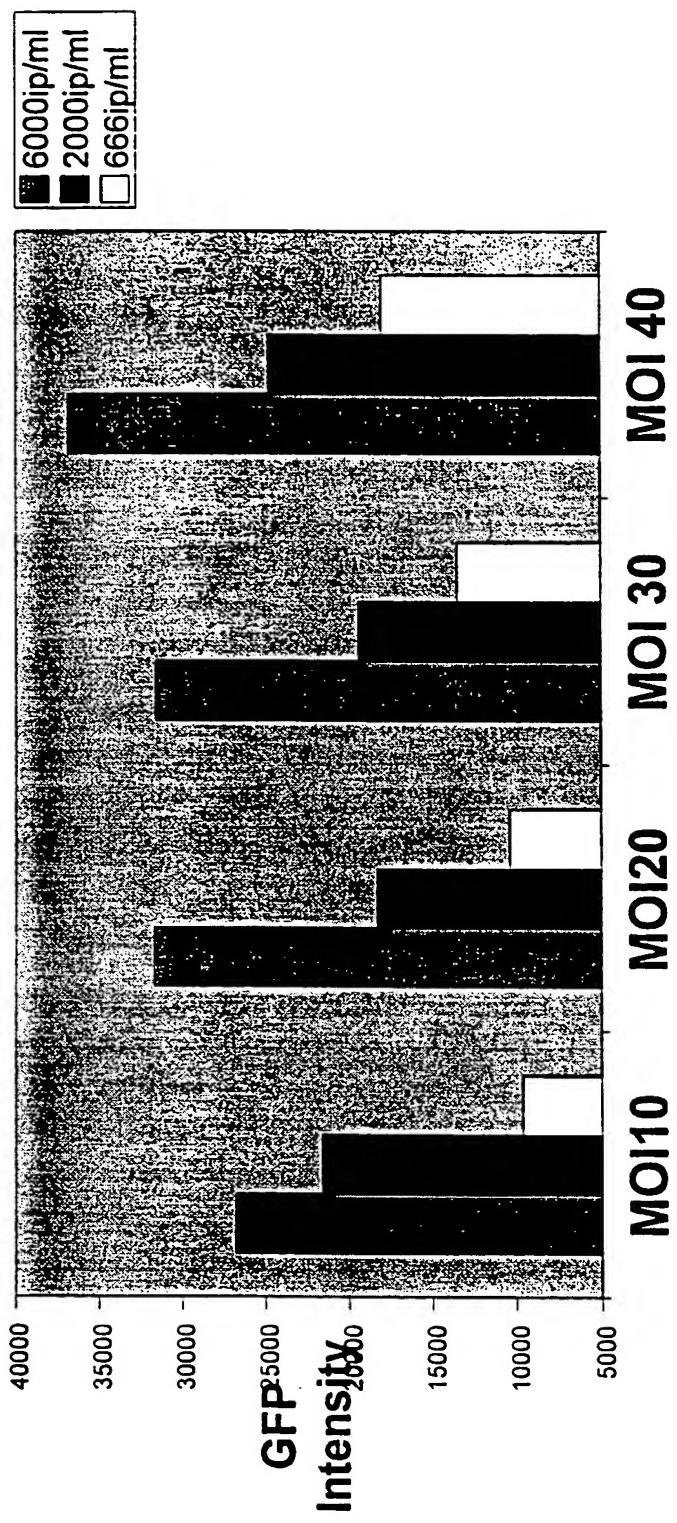


FIGURE 13

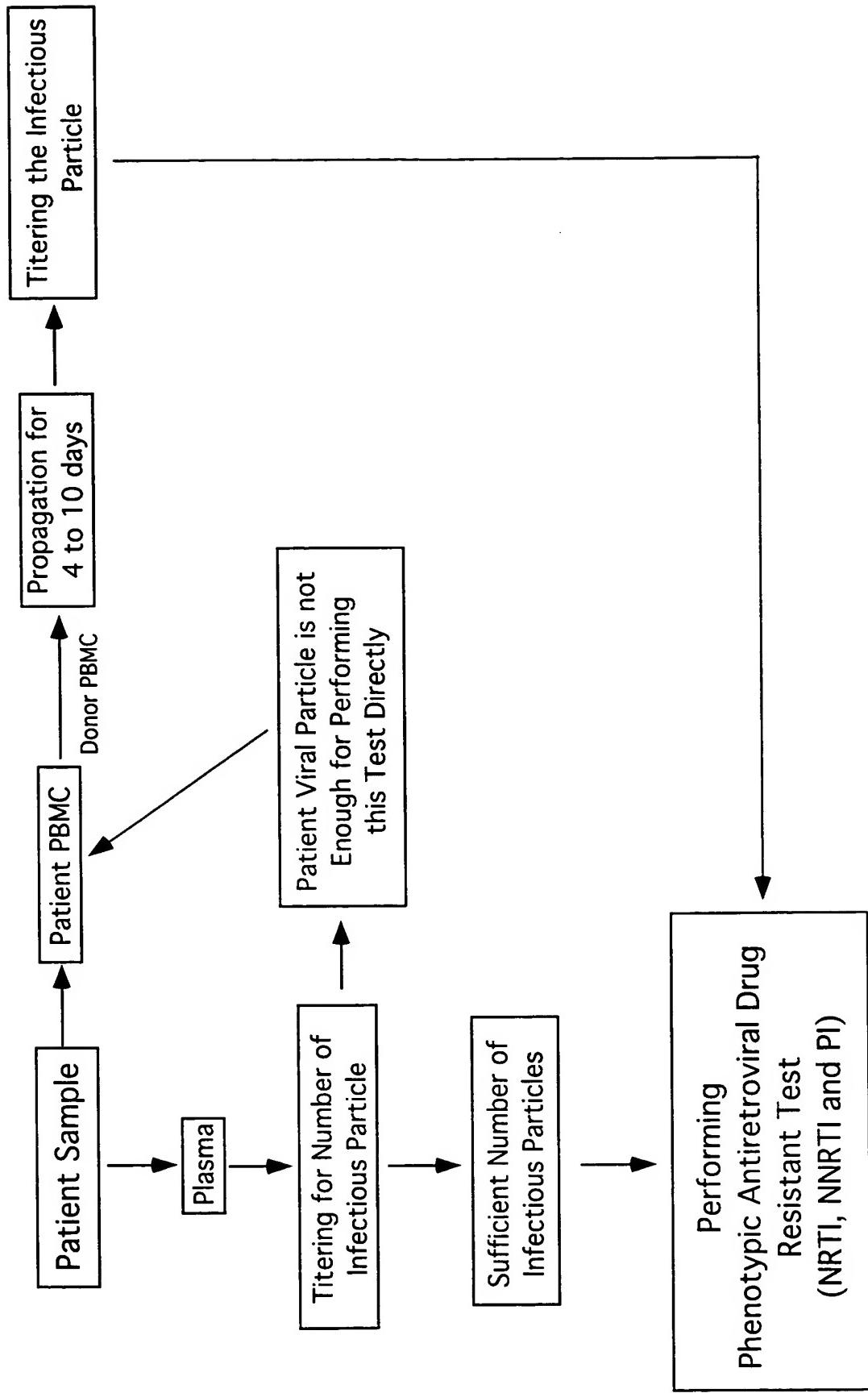


FIGURE 14

Phenotypic Antiretroviral Drug Resistant Test for NRTI and NNRTI

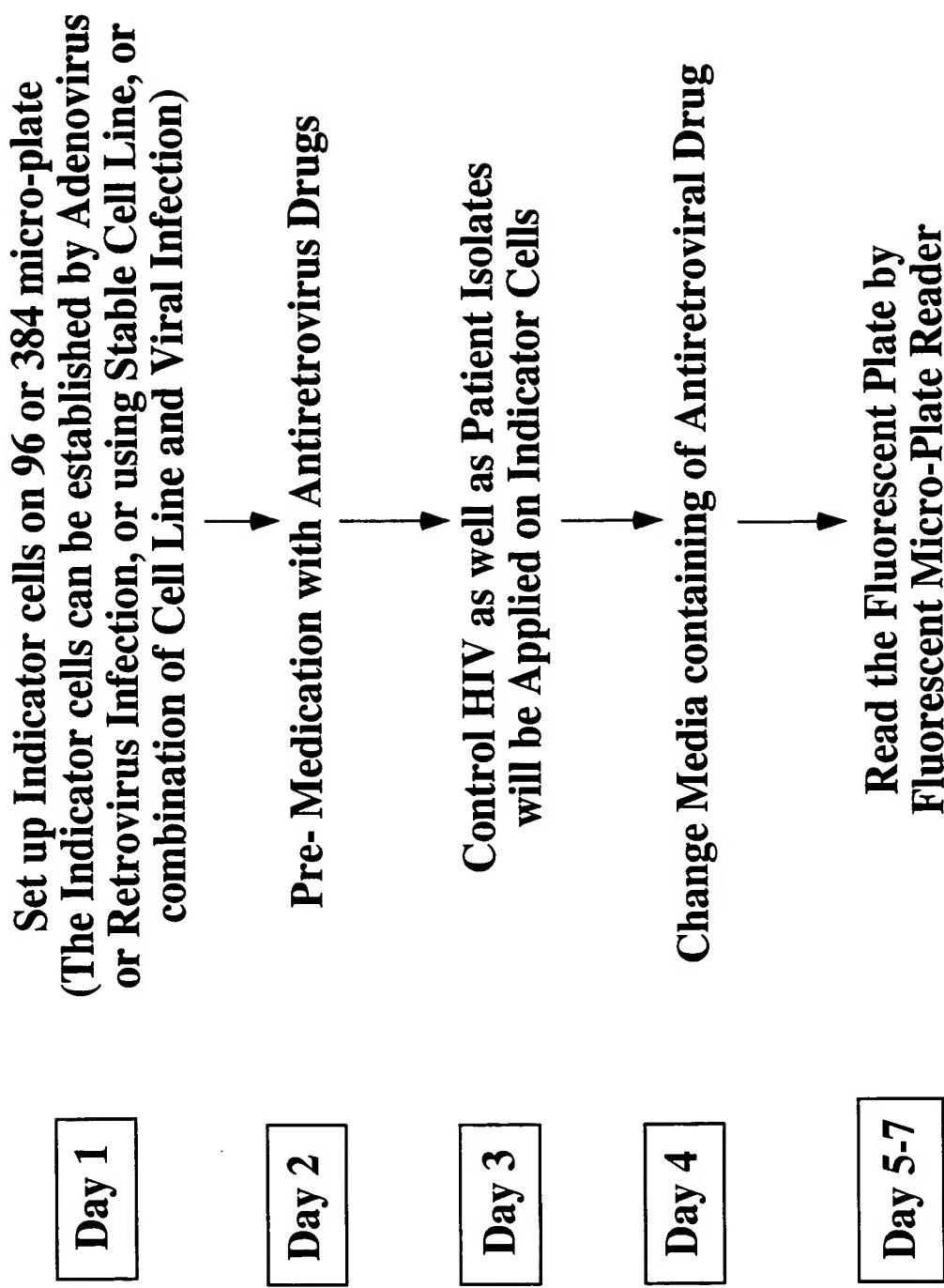


FIGURE 15
HIV DRUG RESISTANCE ASSAY FOR PI

PRIMARY PLATE

Set Up Infection Plate of Cells Containing 3 HIV Receptors with a Sample containing HIV in the Presence of the PI Drug to be tested for a Suitable Period of Time

SECONDARY PLATE

- Day 1 Set Up Indicator Cells Containing 3 HIV Receptors as well as a Reporter Gene for Monitoring HIV Infection



Day 1 Transfer the Supernatant of the Culture in the Primary Plate to the Indicator Cells for Titration of HIV



Day 2 Change Media



Day 3-4 Read Plates by Fluorescent Micro-Plate Reader

FIGURE 16

Phenotypic Antiretroviral Drug Resistant Test

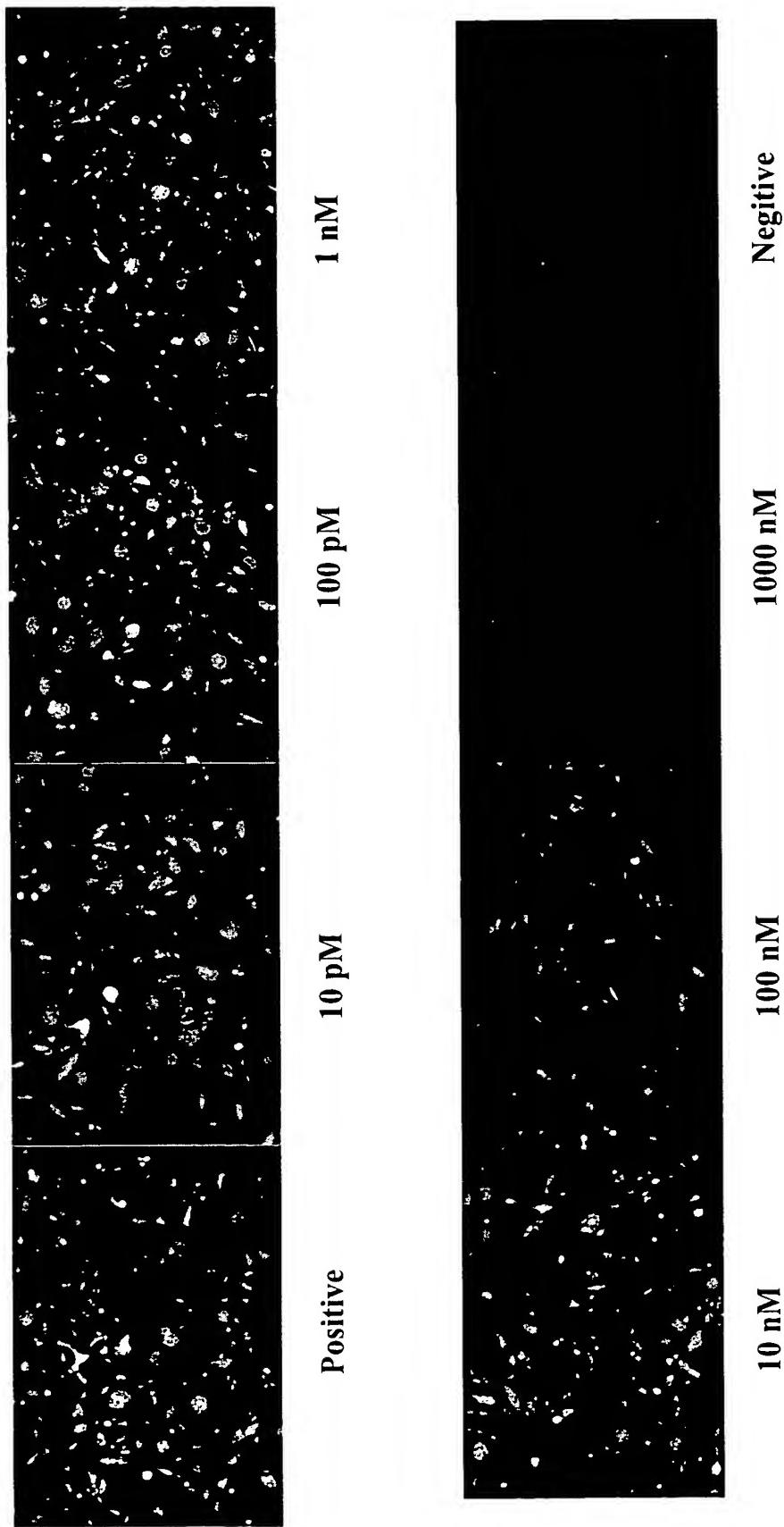


FIGURE 17A

						Patient			
								CS	Drug
								G	
						GenPhar Reference: IC_{50} Values			
		NIH IC_{50} (Other Virus)		NIH IC_{50} (III-B)					
		(Other Cells)		IC_{50} Values					
		Virologic Mean IC_{50}		NIH IC_{50} (Other Virus)					
		(C8D0)		PBMC					

FIGURE 17B

		Virologic Mean IC ₅₀	NIH IC ₅₀ (Other Virus)	NIH IC ₅₀ (III-B) (other Cells)	GenPhar Reference: IC ₅₀ Values	Patient	
Drug Name	Brand Name	(CNDO)	PBMC		JL	b7D	
Zidovudine	Retrovir	0.03	0.05	0.05	0.0008	IC ₅₀	0.074
NRTI	Didanosine	4.57	0.46	8	3.03	Shift	92.5
	Stavudine	0.66	0.009	0.05	0.077	IC ₅₀	57.8
	Zalcitabine	0.68	0.011	0.3	0.115	Shift	19.07591
	Lamivudine	1.77	>100		0.404	IC ₅₀	2.3
	Abacavir	1.74		4	0.827	Shift	29.87
	Tenofovir			0.04	10.3	IC ₅₀	4 d4T
NNRTI	Nevirapine	78		48	45.95	Shift	2.3
	Delavirdine	Rescriptor	32	0.0001	0.1	IC ₅₀	23.5 TNV
	Efavirenz	Sustiva	2	0.003	1.575	IC ₅₀	98,700 NVP
nM					1.01	Shift	2148 DLV
						IC ₅₀	127.1 EFV
						Shift	125.8

FIGURE 17C

FIGURE 17D

Patient C_{50} , Shift, and R^2 Values for GenPhar Tru-Select (G) and Virlogic Phenosense (V) Assay Tests

FIGURE 18A

Dose Response & IC₅₀ Shift Curves for ZDV

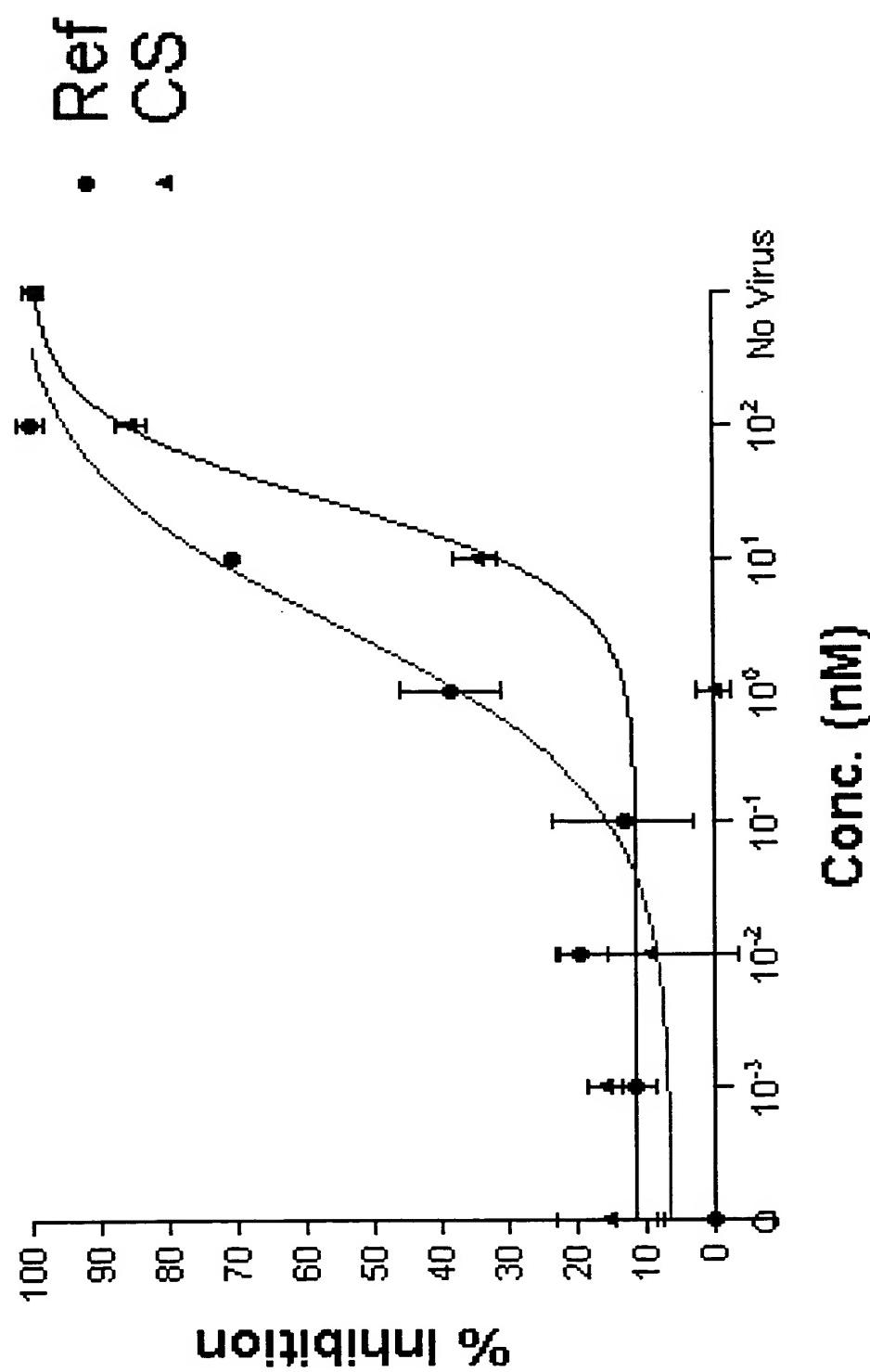


FIGURE 18B

Dose Response & IC₅₀ Shift Curves for NVP

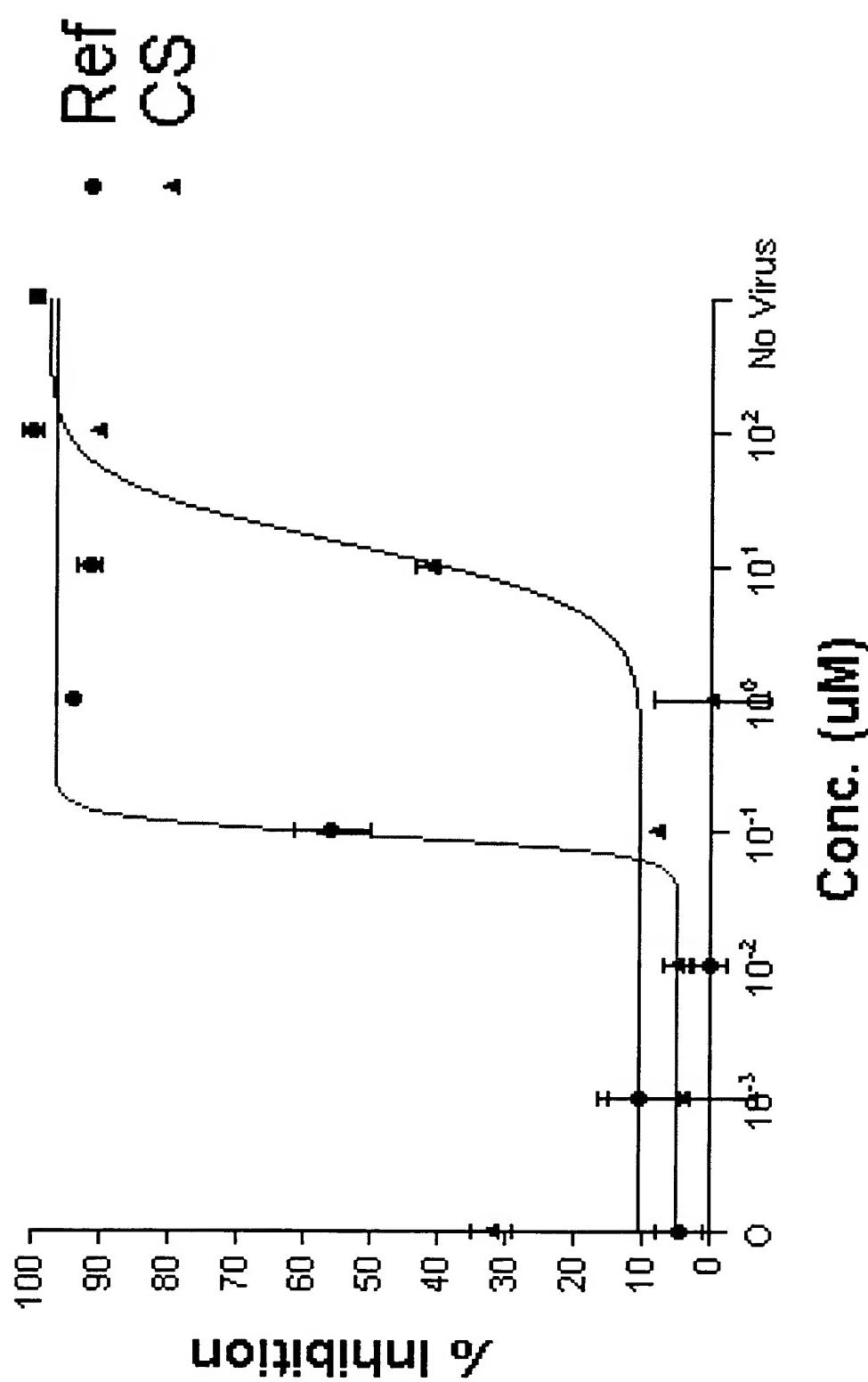


FIGURE 18C

Dose Response & IC₅₀ Shift Curves for RTV

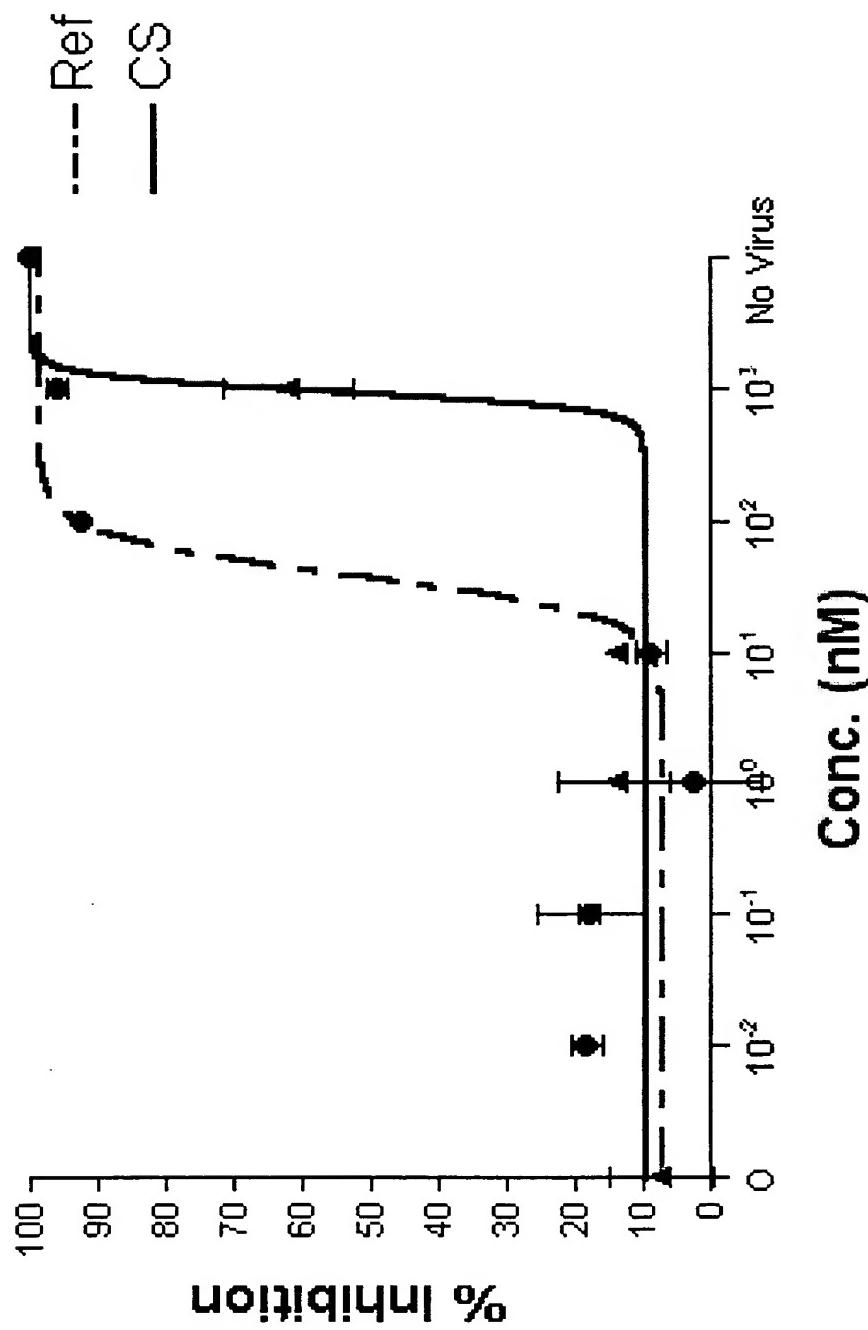
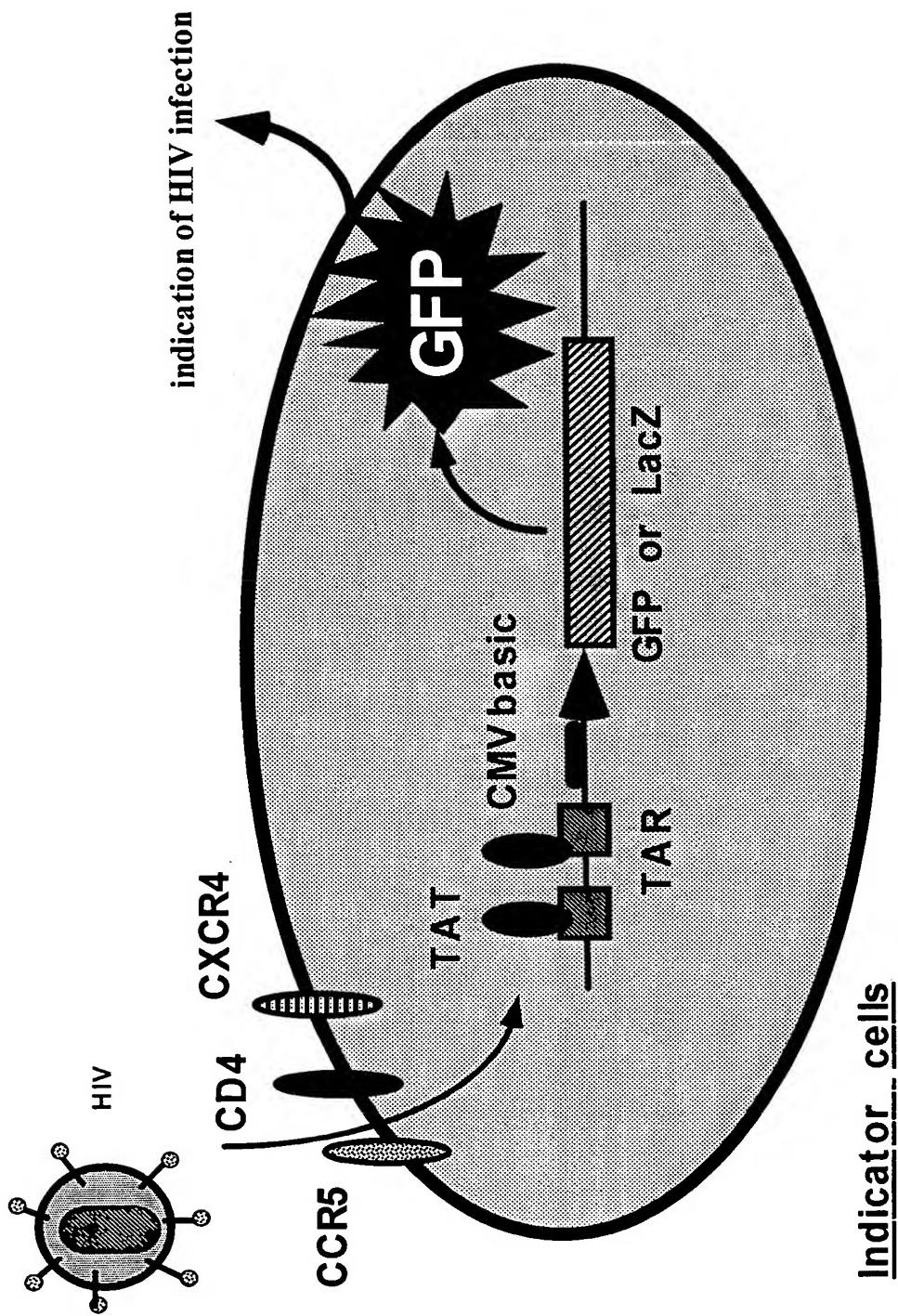


FIGURE 19

Mechanism of the HIV infection indicator cells



Indicator cells

FIGURE 20

HIV DRUG SCREENING ASSAY FOR ESI

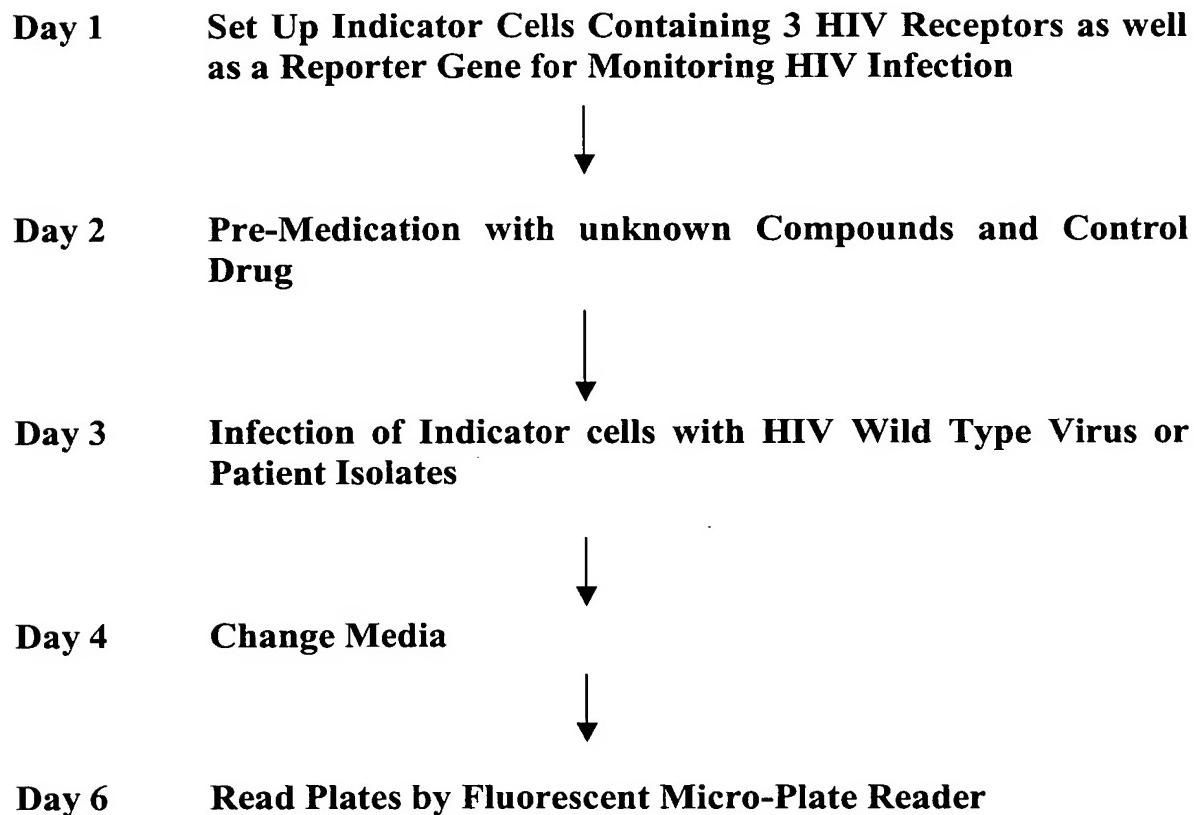


FIGURE 21

HIV DRUG SCREENING ASSAY FOR LSI

PRIMARY PLATE

**Set Up Infection Plate of Cells Containing 3 HIV Receptors
with HIV in the Presence of a Test Agent
for a Suitable Period of Time**

SECONDARY PLATE

**- Day 1 Set Up Indicator Cells Containing 3 HIV Receptors as well
as a Reporter Gene for Monitoring HIV Infection**



**Day 1 Transfer the Supernatant of the Culture in the Primary
Plate to the Indicator Cells for Titration of HIV**



Day 2 Change Media



Day 3-4 Read Plates by Fluorescent Micro-Plate Reader

FIGURE 22

Phase I Layout

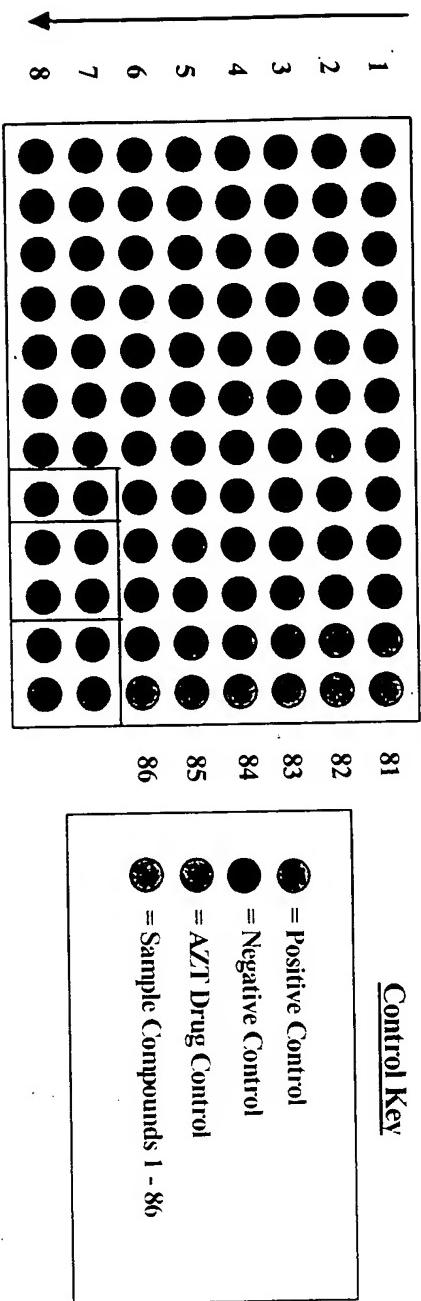


FIGURE 23

Phase II Layout

(Antiviral assay / Cytotoxicity assay)

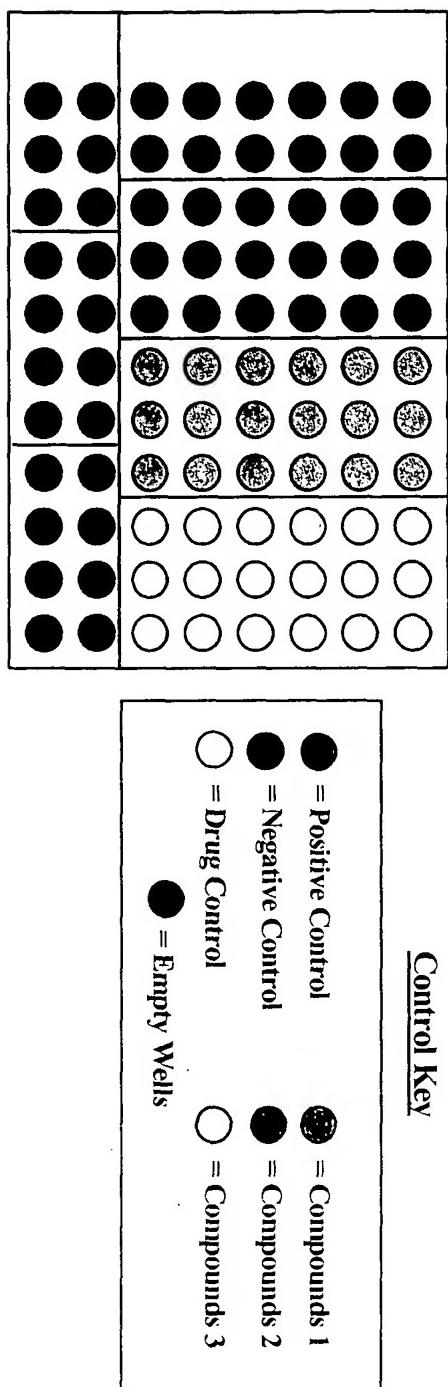


FIGURE 24

Phase III Antiviral Test Layout (WT vs Resistant HIV-1)

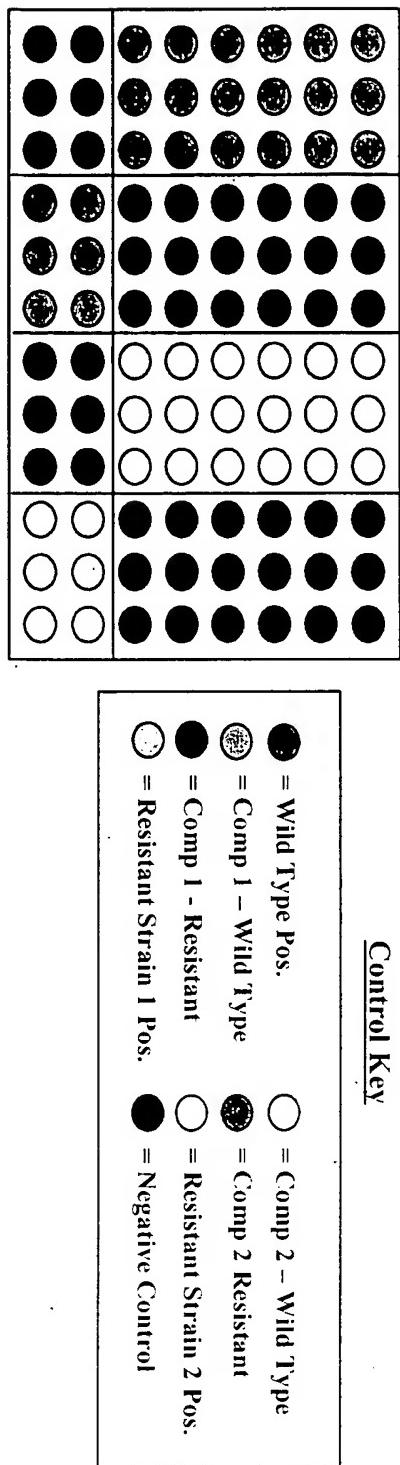
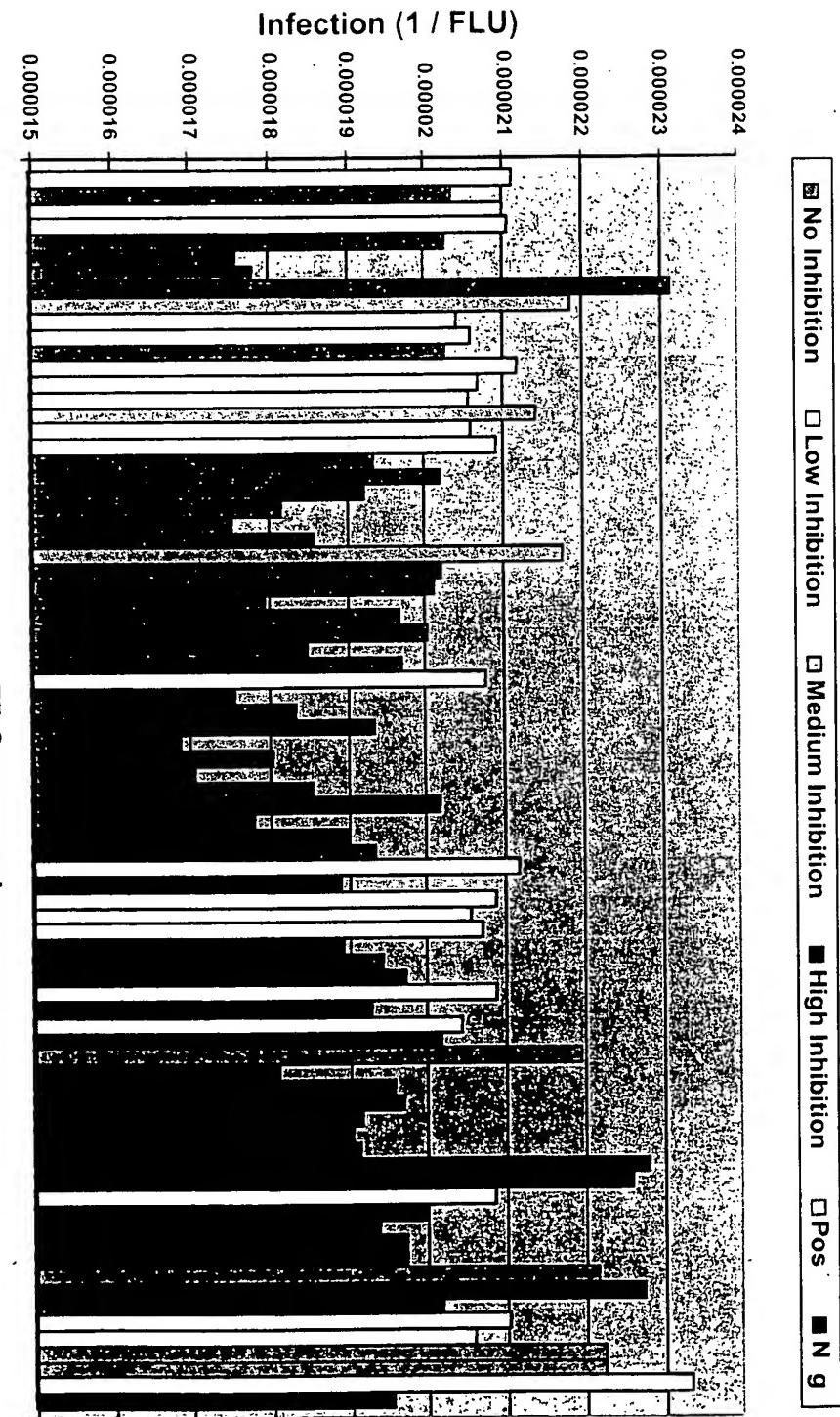


FIGURE 25

Phase I ESI Results



77 Compounds

FIGURE 26

